REMARKS

Claims 1-25 and 27-29 were pending in the application. Claim 19 has been canceled to obviate a rejection that claim 20, a dependent claim, was separated from its parent, claim 16. Claims 36-38 are new. The text of claim 19 has been reintroduced verbatim as new claim 35. Basis for claim 35 can be found in originally filed claims 8, 16 and 18. Applicants request that claim 35 be given the same consideration that claim 19 received. Claims 36-38 depend from claim 35. No new matter has been added with the amendments. Support for claims 36-38 can be found in claim 19 as originally filed.

Request for Clarification

According to the Office Action Summary of August 11, 2004, claims 7, 15 and 19 were allowed. However, these claims were included in those rejected under 35 U.S.C. § 112 in the Detailed Action. Applicants have assumed for purposes of this Amendment, that the Examiner intended to allow claims 7, 15 and 19. For order-of-presentation reasons only, discussed in the paragraph above, claim 19 has been canceled and re-introduced as new claim 35. Applicants wish to thank the Examiner for the indication that the claims are allowed. However, in the event that the Examiner actually intended to reject claims 7, 15 and 19, the arguments set out below are intended to encompass all claims that were rejected; such rejected claims may include claims 7, 15 and 19 (now claim 35). Applicants request clarification on the status of claims 7, 15, and new claim 35 (fka 19).

Claim Objections

The Examiner has objected that dependent claim 20 is separated from claim 16 by independent claim 19. The claims have been amended, so that claim 19 is canceled, to obviate this rejection. Applicants therefore request that this objection be withdrawn.

Specification

The Examiner has objected to the specification as improperly incorporating by reference various documents, specifically US Patent No: 6,310,199 ('199 patent) at page 12 and PCT/US98/01149 published as WO 98/31840 at page 11, for failing to teach with detailed particularity where the specific information intended to be incorporated by reference can be found within the cited documents. In response to the Examiner's previous objection to

the incorporation of the '199 patent, Applicants argued that one of skill in the art would be well able to identify material within the '199 patent that was intended to be incorporated by reference. The Examiner refused to consider these arguments, stating that the level of skill in the art was not dispositive to the issue, because the objection was not an enablement rejection. Applicants respectfully, but strenuously disagree with the Examiner's position.

In the very case that the Examiner cited to support the objection, the Federal Court clearly stated that the standard to be used in determining whether material was referenced with sufficient particularity to be incorporated by reference was one of reasonable skill in the art.

> "Further, the **standard of one reasonably skilled in the art** should be used to determine whether the host document describes the material to be incorporated by reference with sufficient particularity." *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d 1673. (Emphasis added)

Applicants, therefore, reiterate the previously articulated arguments that one of reasonable skill in the art would have no difficulty in identifying the material of the '199 patent intended to be incorporated by reference, and respectfully request that the Examiner re-consider those arguments on the merits. The merits of these arguments include that while Applicants incorporated the entire '199 Patent by reference, Applicants refer specifically to "ion exchange ligands and pH dependent ion exchange matrices which incorporate such ligands." With all due respect, it is well within the ability of one skilled in the art to identify that material within the '199 Patent that relates to pH dependent ion exchange particles.

Clearly, the information to be incorporated by reference is not an obscure statement buried in the text of the '199 patent, but rather the relevant parts are plainly described in the specification of the instant application. One skilled in the art would appreciate that Applicants were intending, for example, to refer to Examples 3, 5, or 7 of the '199 Patent. Furthermore, the specification of the instant application itself describes the preparation of pH dependent ion exchange particles (e.g., see Example 3). Thus, incorporation of the '199 patent by reference was not necessary to describe the claimed invention or to provide an enabling disclosure. Those requirements were met by the specification of the instant application as originally filed.

Similarly for the reference made to PCT/US98/01149, published as WO 98/31840, on p.11 of the instant application, Applicants refer specifically to "methods of adsorption and

desorption of target nucleic acids to silica magnetic particles." Again, one of skill in the art would have no difficulty in identifying the material intended to be incorporated by reference in PCT/US98/01149. The specification of this application itself also describes methods of adsorption and desorption of target nucleic acids to silica magnetic particles, for example, on page 10, line 12 to page 11, line 3, and in Example 7. Incorporation of the patent publication was not necessary to describe the claimed invention or to provide an enabling disclosure. Those requirements were met by the specification of the instant application as originally filed.

In the interests of furthering prosecution, Applicants supplement these arguments with a Declaration, under 37 CFR § 1.132, from Dr. Rex Bitner, an inventor who is skilled in the art, that one of skill in the art would have no difficulty in identifying which portions of the '199 patent and the WO 98/31840 publication were incorporated by reference. Several observations may be made from Dr. Bitner's Declaration:

1. Dr. Bitner observes at paragraph 4 that one of reasonable skill in the art would have:

> "no difficulty identifying the material intended to be incorporated by reference in identifying the documents that were incorporated by reference...." (emphasis supplied)

The reason Dr. Bitner is of this opinion is that the '199 patent, while being incorporated generally, was focussed by referring to "ion exchange ligands and pH dependent ion exchange matrices which incorporated such ligands"..... In other words, one referring to the '199 patent incorporated by reference was not sent on a random search but was given specific guidance as to what to look for. As is noted in paragraph 5 of Dr. Bitner's Declaration one skilled in the art would, at the very least, appreciate that Examples 3, 5 or 7 of the '199 patent were intended.

2. At paragraph 5 of Dr. Bitner's Declaration Dr. Bitner indicates "accordingly, it is my belief that incorporation of the patent was not necessary to describe the claimed invention or to provide an enabling disclosure." Most certainly that is Applicants' position, viz., that whether the Examiner agrees with our application of the incorporation-by-reference rules or not, the present specification is, itself, sufficient to meet all of the requirements of the patent statute without any incorporated information.

3. In paragraph 6 of Dr. Bitner's Declaration an analysis of the portions of PCT/US98/01149 (referred to as PCT 01149 in Dr. Bitner's Declaration) is discussed. Again, while a general incorporation by reference was made that general incorporation by reference was focused to indicate "methods of absorption and desorption of target nucleic acids to silica magnetic particles".... Thus, Dr. Bitner concludes that one of ordinary skill in the art would appreciate that at least Examples 4, 5 and 6 of PCT 01149 were intended.

In view of the foregoing, Applicants' respectfully request withdrawal of the objection that the indicated documents were improperly incorporated by reference.

Request for Information

The Examiner raised an issue of public use or on sale activity in this application and requested information pertaining to the manufacture and sale of pH-dependent ion exchange particles as well as silica magnetic particles encompassed by the methods of claims 1 and 21, including information relating to the manufacture and sale of MagneSil™; silica beads used in Wizard™ *Plus* Plasmid Purification Systems, the MagneSphere® Technology Magnetic separation stand, the Poly A Tract® Series 9600TM Multi-Magnet, the Magnetight Separation Stand and the Dynal Magnetic Particle Concentrator. The Examiner further requested that a copy of each publication authored or co-authored by any of the inventors that describes the disclosed subject matter of claims 1-25 and 27-29, and the names of any products or services that have incorporated the claimed subject matter.

Applicants point out to the Examiner that two of the products listed above are not those of the Applicants' employer, Promega Corporation. The Dynal Magnetic Particle concentrator is a product of Dynal Biotech, headquartered in Oslo, Norway; and the Magnetight separation stand is a product of EMD Biosciences, Novagen Brand of Madison, Wisconsin. In addition, Applicants have not sold pH-dependent ion-exchange particles. Consequently, Applicants have no public use or sales activity documents pertaining to these products.

Applicants otherwise enclose the information requested by the Examiner, listed on form PTO 1449B PTO. We trust that the Examiner will agree with our assessment, viz., that there has been no public use or on sale activity pertinent to t he subject matter of this application.

Rejections under 35 U.S.C. § 112, first paragraph, written description

Claims 1-25 and 27-29 are rejected for failing to comply with the written description requirement of 35 U.S.C. § 112. The Examiner asserted that only glycidyl-histidine and glycidyl-alanine silica magnetic particles were described. The Examiner acknowledged that the specification states that other embodiments would be apparent to those skilled in the art, but asserts that with the exception of glycidyl-histidine and glycidyl-alanine silica magnetic particles, the particles have not been adequately described.

The Manual of Patent Examining Procedure states that for determining the standard for compliance with the written description requirement:

> The subject matter of the claim need not be described literally (i.e., using the same terms or in *haec verba*) in order for the disclosure to satisfy the description requirement.
> MPEP § 2163.02

It is therefore not necessary for Applicants to describe the elements of the claims literally in order to comply with the written description requirement.

The Examiner has pointed out that the specification, on page 16-17, discloses "[o]ther magnetic silica particles and their use in the present method to concentrate cells, to clear solutions of disrupted biological material, and to isolate target nucleic acids from disrupted biological material will be apparent to those skilled in the art of chromatographic separations and molecular biology." The Examiner suggested that Applicants were attempting to satisfy the written description requirement through obviousness. Applicants respectfully disagree with the Examiner's interpretation of this statement. The Manual of Patent Examining Procedure states that:

> To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that **one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention**.

MPEP § 2163 (I) (emphasis added)

In the instant application, Applicants point to the above cited language from the specification merely as evidence that one of reasonable skill in the art could reasonably

conclude that Applicants were in possession of the claimed invention. Disclosure of the types of particles envisioned as suitable for use in the invention is provided at page 10, lines 32 to page 14, line 3. Additionally, Applicants point to language throughout the specification, wherein particles other than glycidyl-histidine and glycidyl-alanine silica magnetic particles are described. For example, BioMag® particles (page 3, lines 1-11), MagneSil™ particles (page 3, lines 1-11 and 23-28; page 6, lines 23-24 and 28-29; page 15, lines 14-24; Example 7); silica magnetic particles disclosed in PCT/US98/01149 and US Patent 6,310,199 (page 4, lines 12-16); ion-exchange and pH-dependent silica magnetic particles (page 9, lines 27-32; page 10, lines 1-7); and silica magnetic particles (Example 6) (all page numbers refer to the application as originally filed).

Therefore, in addition to the description of glycidyl-histidine and glycidyl-alanine silica magnetic particles in the Examples, one skilled in the art would appreciate that Applicants had possession of other magnetic particles and would reasonably conclude that Applicants were in possession of the claimed particles.

Furthermore, Applicants respectfully assert that there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims"). Applicants respectfully assert that the Examiner has not presented any evidence suggesting why those of skill in the art would not recognize in the disclosure, a description of Applicants' invention defined by the claims. In view of the forgoing arguments, Applicants respectfully request that the Examiner's objections be withdrawn and that the claims be allowed.

The Examiner has also objected to claim 21 as failing to meet the written description requirement, because the claimed isolation of "target nucleic acid" has been interpreted to encompass nucleic acids that have a specific sequence, as well as the isolation of a specific class of nucleic acids. Applicants respectfully assert that the Examiner has misinterpreted the term 'target nucleic acid' as it is defined in the specification on page 8, line 31 to page 9, line 2. The specification there states that "[t]he term "target nucleic acid" as used herein refers to any particular species of nucleic acid to be isolated using magnetic particles according to a method of the present invention. The target nucleic acid is preferably at least 20 nucleotides

long, more preferably at least 100 nucleotides long, and most preferably at least 1000 nucleotides long."

The Manual of Patent Examining Procedure states that:

> Consistent with the well-established axiom in patent law that a patentee or applicant is free to be his or her own lexicographer, a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the written description clearly redefines the terms.

MPEP 2173.05(a) III

Being free to be their own lexicographers, Applicants have defined the term "target nucleic acid" very clearly in the specification to encompass a specific species of nucleic acid rather than a specific sequence. Applicants do not suggest that their use of the term "target nucleic acid" is used contrary to its ordinary meaning. However, even if the Examiner were to interpret it as being used in such a contrary way, that use is permitted because the term is clearly defined in the written description of the application. Applicants therefore request that the objection be withdrawn and that claim 21 be allowed.

Rejections under 35 U.S.C. § 112, first paragraph, enablement

The Examiner rejected claims 1-6, 8-14, 16-18, 20-25 and 27-29, for failing to comply with the enablement requirement of 35 U.S.C. §112, however, in the office action summary, claims 7, 15 and 19 (now claim 35) were allowed. Applicants request clarification on which claims were rejected for enablement. Applicants have assumed that the Examiner intended to allow claims 7, 15 and 19 (now claim 35) and assert the following arguments for claims 1-6, 8-14, 16-18, 20-25 and 27-29.

The Examiner asserted that the rejected claims encompass performing all of the steps of the recited methods under the same conditions, and states that the disclosure reveals that different conditions are required to achieve each of the various forms of binding. The Examiner has also asserted that the specification has provided only two versions of essentially the same particle that can be used in the claimed methods, which fails to enable the scope of the claims.

Applicants assert that there is sufficient support in the specification that would enable one of skill in the art to practice the invention, without undue experimentation. Factors to be considered when determining whether undue experimentation is required include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

MPEP § 2164.01(a)

The level of skill in the art for biotechnology is generally considered to be high. Furthermore, Applicants have provided ample direction to enable one skilled in the art to perform the steps of the recited methods. Applicants have provided working examples, in Examples 5, 6, 7, 8, 9 and 10, which describe the binding conditions and which provide guidance to enable one of skill in the art to practice the invention. Applicants, also, refer the Examiner to enabling guidance and teaching throughout the specification. For example, guidance and teaching of the conditions required to accomplish various forms of binding can be found at page 9, line 25 to page 11, line 11. Guidance as to the pH and presence of agents promoting formation of the complex can be found at page 10 line 22 to page 11 line 8; page 12, lines 1-10; page 14, lines 15-32; and page 15, lines 4-11 (all page numbers refer to the application as originally filed).

Furthermore, Applicants point to language throughout the specification which would enable one skilled in the art to use a variety of silica magnetic particles. For example, page 3, lines 1-11 and 23-28; page 4, lines 1-7 and 12-16; page 6, lines 23-24 and 28-29; page 7, lines 3-4, 6-7 and 30-33; page 8, lines 9-27; page 9, lines 27-32; page 10, lines 1-7, 12-15 and 29-32; page 11, lines 1-32; page 12, lines 1-30; page 13, lines 1-32; page 14, lines 1-3, page 15, lines 14-24; page 21, lines 19-31; page 22, lines 1-15; page 23, Table 1; page 24, lines 19-25 and 27-30; page 25, lines 1-15, Table 2 and lines 24-26; page 32, lines 10-31; page 33, lines 1-20; page 35, Table 4 (all page numbers refer to the application as originally filed).

In view of the arguments above, Applicants assert that the scope of the claims is fully enabled by the disclosure. Applicants request that the rejection for failure to comply with the § 112 enablement requirement be withdrawn, and that all claims be passed to issue.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-6 were rejected as indefinite, for failing to particularly point out and distinctly claim the subject matter of the invention. The Examiner objected that claim 1 was indefinite as to whether the pH dependent particles, or whether just the silica magnetic particles are coated with a siliceous oxide having a hydrous siliceous adsorptive surface. This objection to claim 1 had already been made the Office Action mailed 11/13/2003, in response to which, Applicants argued that the claim was not indefinite. In the most recent action, the Examiner apparently did not consider Applicants' arguments in the amendment mailed April 13, 2004, but reiterated the same objection towards claim 1 and its dependent claims 2-6.

The Manual of Patent Examining procedure states:

> Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicant's argument and answer the substance of it.

MPEP § 707.07(f)

Applicants respectfully assert that the Examiner is required to consider the arguments made in Applicants' 4/13/2004 response to the earlier Office Action mailed 11/13/2003, which are repeated below.

"The particles to which the Examiner refers form a Markush group, which was introduced by Examiner's amendment mailed with a Notice of Allowance on September 5, 2000. The Markush group is reproduced below:

> "wherein said magnetic particles are selected from the group consisting of (1) pH dependent ion exchange particles and (2) silica magnetic particles consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface..."

Applicants believe that the two types of particles are clearly separated by numerals (1) and (2), and that the "consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface..." is intended to refer only to the silica magnetic particles. This construction is supported by the fact that the pH dependent ion exchange particles, even pH dependent ion exchange particles comprising a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface, would be modified such that the essential character would be changed."

Based on the above arguments, Applicants request that the objection to claim 1, and dependent claims 2-6, be withdrawn, and that claims 1-6 be allowed.

Claims 1, 8 and 21 were rejected as indefinite with respect to what constitutes the metes and bounds of "consisting essentially of," in view of the teachings of the specification. Dependent claims 22-25 and 27-29 were similarly rejected. The Examiner has asserted that the metes and bounds of surface modification are less than clear.

The Manual of Patent Examining Procedure states:

> The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original)

MPEP § 2111.03

The Examiner noted that the presence of glycidyl-histidine or glycidyl-alanine is considered a significant modification of the hydrous siliceous surface. Applicants agree that such particles are not intended to be within the metes and bounds of "silica magnetic particles consisting essentially of a magnetic core coated with a siliceous oxide having a hydrous siliceous oxide adsorptive surface." Silica magnetic particles are defined in the specification on page 8, lines 9-11, as "refer[ring] to paramagnetic particles comprising a superparamagnetic core coated with siliceous oxide, having a hydrous siliceous oxide absorptive surface." The Examiner stated that in the absence of alternative embodiments, the metes and bounds of surface modification is less than clear. With due respect, it is not necessary to disclose alternative embodiments in the specification in order for the metes and bounds of "consisting essentially of" to be clear. Rather, the use of the term "consisting essentially of" will include, in addition to the specified materials, those that do not materially affect the basic and novel characteristics of the claimed invention. There is no requirement that materials that might materially affect the basic and novel characteristics of the claimed invention be specified.

In view of the arguments above, Applicants request that the Examiner withdraw the objections and allow claims 1, 8 and 21, and dependent claims 22-25 and 27-29.

Non-statutory double patenting rejection

The Examiner provisionally rejected claims 15-25 and 27-29 under the judicially created doctrine of obviousness-type double patenting. In compliance with 37 C.F.R. 3.37(b) Applicants concurrently file a terminal disclaimer, signed by the assignee's attorney of record. Applicants therefore request that the rejection of claims 15-25 and 27-29 for double-patenting, be withdrawn.

As the application is now in condition for allowance, Applicants respectfully request withdrawal of all objections and rejections and allowance of all claims.

This response is accompanied by check in the amount of $1,330.00 to cover the fees required under 37 C.F.R. 1.17(a)(3) ($1,020.00 for 3-mo. extension request + $180.00 Supplemental IDS + $130.00 for Statutory Disclaimer37 CFR 1.20(d). No other fee is believed to be due in connection with this submission. If additional fees are owed, please charge such fee to deposit account number 50-0842.

Respectfully submitted,

Grady J. Frenchick 2/11/05

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